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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/367,859	09/02/1999	JAMES SAMSOONDAR	5352-051	4860

7590 08/13/2002

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EXAMINER
SODERQUIST, ARLEN

ART UNIT	PAPER NUMBER
1743	

DATE MAILED: 08/13/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

1 D

Office Action Summary

Application No.	Applicant(s)
09/367,859	Samsoondar
Examiner	**Art Unit**
Arlen Soderquist	1743

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Jun 3, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1 and 5-22* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1 and 5-22* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. Claims 1 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claim 1 an interferant is a relative thing since it interferes with the analysis of another component of a sample. Since there are no steps for measuring an analyte in claim 1 the process is either lacking steps related to the analysis of the analyte or the interferant is actually the analyte for claim 1 and the claims which are dependent therefrom. For examination purposes the interferant will be treated as the analyte since calling it an interferant does not change the fact that it is the only thing that a concentration is being determined. The analyte appears to play no part in the analysis which is occurring in claim 1 or the claims dependent therefrom.

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1 and 5-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sagusa in view of Gimpel, Simon and Christenson, Leissing or Mullins. In the patent Sagusa teaches a colorimetric method for samples including interfering chromogens. Color former is added to blood serum sample color it, and measurements for specific components are determined based on the light absorbance caused by coloring. For one sample, a differential light absorbance between two wavelengths at each of long wavelength region, middle wavelength region and short wavelength region within a visible wavelength band is determined. The degree of chyle is

determined from the measurements for the long wavelength region, the degree of hemolysis is determined from the measurements for the middle wavelength region, and the degree of icterus is determined from the measurements for the short wavelength region. The measurements for the specific components are then corrected by the degree of chyle, degree of hemolysis and degree of icterus to obtain highly correct measurements. Sagusa does not teach interference by blood substitutes, using derivative spectroscopy in the correction equation or detection of pseudohemolysis.

In the abstract Christenson discusses hemoglobin based blood substitutes and their interference with routine chemical tests.

In the abstract Leissing discusses modification of clinical chemistry methods to overcome interferences from diaspirin crosslinked hemoglobin (DCLHb).

In the paper Mullins discusses effects of Fluosol-DA (artificial blood) on clinical chemistry tests and instruments. Artificial blood must be added to the list of therapeutic agents that produce interference with diagnostic laboratory tests. Fluosol-DA (Alpha Therapeutic Corp., Los Angeles, CA), a stable 20% emulsion of perfluorocarbons in aqueous medium, is being evaluated in clinical trials as a blood substitute in the United States. They investigated its effects in blood and serum samples on test results and instruments in the clinical chemistry laboratory. The 20% emulsion was added to blood or serum specimens in amounts corresponding to the replacement of in-vivo plasma volumes of 10-50%, concentrations that would be expected in blood samples obtained from patients who have received Fluosol. Observed interferences mimicked those caused by high triglyceride concentrations in serum specimens: interference with chemical reactions and generation of spurious absorbance readings because of turbidity. These types of errors are often additive, and the cumulative effect may cause either erroneously high or low values for the analytes concerned. Because Fluosol may be used widely, although infrequently, for patients refusing blood transfusions on religious grounds and for patients with rare antibodies to red blood cells who require transfusion, laboratories analyzing specimens containing Fluosol should be aware of the potential errors.

In the paper Gimpel teaches a reference interval for the bilirubin excess in cerebrospinal fluid by derivative spectrophotometry. The value of the bilirubin excess can be a useful aid for recognizing blood from hemorrhage in cerebrospinal fluid. One of the parameters needed for the calculation of the bilirubin excess is the total bilirubin concentration in cerebrospinal fluid. A method for measuring total bilirubin in cerebrospinal fluid is presented, based on diazotization of bilirubin according to Jendrassik-Grof, combined with multiwavelength first-derivative spectrophotometry. This bilirubin assay allows determination of total bilirubin concentrations as low as 0.045 μmol/L. This method also enables a correlation for oxyHb interference. The value of the bilirubin excess was calculated for patients not showing any neurological disorder. A reference interval of 0.07 ± 0.06 μmol/L was calculated for the bilirubin excess. Particularly relevant to the instant claims is the calculations and equations shown in the right column of page 218.

In the paper Simon discusses a "pseudo-hemolytic" transfusion reaction caused by intravenous iron-dextran therapy. Intravenous iron-dextran therapy can cause a red-brown discoloration of the plasma, simulating a hemolytic transfusion reaction. A rapid and simple test to differentiate between true hemolysis and plasma discoloration due to circulating iron-dextran complexes is described.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to include substances such as blood substitutes recognized by Christenson, Leissing or Mullins as interfering substances into the Sagusa correction method because of the recognized possibility for interference with clinical chemistry tests and the projected use of these substances in humans. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the Sagusa method to differentiate between true hemolysis and plasma discoloration due to circulating colored substances as taught by Simon because of the ability to select wavelengths that will allow the effects of one chromogen to be removed from another chromogen as taught by Sagusa and the need to differentiate between true hemolysis and plasma discoloration due to circulating substances as taught by Simon. It would have been obvious to one of ordinary skill in the art at the time the invention was made to use a derivative

spectroscopic method as shown by Gimpel for correction in the Sagusa method because of the ability to differentiate between interfering substances such as the hemoglobin and bilirubin of Gimpel. Determination of specific wavelengths would be a results effective variable which has been held to be within the skill of the routineer in the art by the Courts (see *In re Boesch*, 205 USPQ 215 (CCPA 1980)).

4. Applicant's arguments filed June 3, 2002 have been fully considered but they are not persuasive. Relative to the lack of clarity, it appears that applicant is trying to claim a general method of determining the concentration of a substance in the presence of other substances which interfere with the measurement or overlap the spectrum. The rejection is attempting to show that the language used will not distinguish a substance which interferes with another substance and the substance that is interfered with by other substances unless there are steps directed to the measurement of the substance that is designated as the analyte in addition to the steps for measuring the interfering substance. Thus claims 1 and 7 are being treated without a determination if the substance being measured is the interfering substance or the analyte. In other words calling something an interferant fails to distinguish the substance from an analyte when it is the only substance that is required to be measured by the claimed steps. Thus applicant's arguments that a reference is not teaching the measurement of a "selected interferant" is without merit because there is not any requirement to measure the presence or concentration of another compound as the "analyte". Another way of saying this is hemoglobin can act as both an interfering substance for an analyte such as glucose but it can also be an analyte as in claim 21. The only way for hemoglobin to be an interfering substance is if one is also trying to measure another compound that the hemoglobin signal overlaps. Since claim 1 only requires one to measure the presence of one substance the measured substance cannot be called an interfering substance because it is the only substance which is being measured. Another way to say it is one of skill in the art would not know whether they are infringing one the scope of claim 1 if they measure the presence of hemoglobin or any other analyte since they can interfere with the measurement of any substance for which they have a spectral overlap. Nor can applicant identify whether or not the measured substance is an interfering substance until the measurement is used

to correct or adjust the measurement of another substance which spectrally overlaps the first substance. Another example of this is found with bilirubin which is found in both the list of interfering substances and analytes on page 4 of the response.

Examiner agrees that no single reference anticipates the claims. However, the Sagusa reference clearly teaches methods for dealing with interfering compounds in analyses in blood samples. Thus a teaching that blood substitutes are known or expected to interfere with chemical tests as found in Christenson, Leissing or Mullins would have motivated one of skill in the art to use the methods of Sagusa to overcome interference from the blood substitutes in the circumstances that the blood substitutes would have been expected to interfere. In the same manner the teachings relative to the pseudo-hemolytic behavior of the iron-dextran therapy substances would have motivated one of skill in the art to make measurements to distinguish or differentiate between real hemolysis and the pseudo-hemolysis caused by a substance or medication that was being administered to a person or patient because it would allow the proper care to be given. The cited and applied Gimpel reference clearly shows use of first derivative spectroscopy to remove the influence of interfering substances in a manor being claimed. Relative to the addition of a color producing reagent in Sagusa examiner points to the list of analytes on page 4 of the response and asks how many of them are measured using a color producing agent? By the argument that the instant claims do not require the addition of a color producing reagent, is applicant limiting the claims to analytes which are only measured without addition of a color producing agent? If so the claims should be closed language. Currently the claims are open and the Sagusa reference is completely within the claim scope. The list of interfering substance the Sagusa is trying to correct for includes (column 1, lines 21-25) hemoglobin, bilirubin and turbidity which are all part of the list of interfering substances found on page 4 of the response.

5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

6. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additional art relates to correction of spectra using first derivative spectroscopy.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose telephone number is (703) 308-3989. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

For communication by fax to the organization where this application or proceeding is assigned, (703) 305-7719 may be used for official, unofficial or draft papers. When using this number a call to alert the examiner would be appreciated. Numbers for faxing official papers are 703-872-9310 (before finals), 703-872-9311 (after-final), 703-305-7718, 703-305-5408 and 703-305-5433. The above fax numbers will generally allow the papers to be forwarded to the examiner in a timely manner.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0661.

Arlen Soderquist

August 9, 2002

ARLEN SODERQUIST
PRIMARY EXAMINER